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The Kidney in Multiple Myeloma

These discussions are selected from the weekly staff conferences in the Department of Medicine, University of California, San Francisco. Taken from transcriptions, they are prepared by Drs. David W. Martin, Jr., Associate Professor of Medicine, and Robert C. Siegel, Associate Professor of Medicine and Orthopaedic Surgery, under the direction of Dr. Lloyd H. Smith, Jr., Professor of Medicine and Chairman of the Department of Medicine. Requests for reprints should be sent to the Department of Medicine, University of California, San Francisco, CA 94143.

DR. SMITH:* *At medical Grand Rounds this morning we will focus on the renal complications of multiple myeloma. Dr. Jane Melnick will present the case.*

Case Summary

DR. MELNICK:† The patient is a 90-year-old white man transferred from another hospital for evaluation of obtundation, anuria, fever and anemia. The patient had been in his usual state of excellent health until three weeks before admission. While vacationing in Hawaii, he sustained a spontaneous fracture of the left humerus. This was accompanied by fatigue and malaise. One week before admission, with an increase in his constitutional symptoms, he entered the first hospital; he was at that time ambulatory and oriented. Laboratory studies showed a hematocrit reading of 28 percent, a blood urea nitrogen (BUN) value of 38 mg per dl and a calcium value of 10.6 mg per dl. A barium enema study showed diverticulosis. An intravenous pyelogram which was undertaken to rule out obstruction showed decreased dye excretion, but a normal caliceal system insofar as it was visualized. Subsequent to the intravenous pyelogram, urine output was noted to fall to less than 10 ml per hour and this was accompanied by fever and a gradual deterioration in mental status until the day before transfer when the patient became unresponsive. A x-ray film of the chest was said to show a right lower lobe infiltrate; urine culture showed 10^5 Escherichia coli. Therapy was begun with intravenous administration of ampicillin and the patient was transferred to the University of California Medical Center 24 hours later.

Vital signs on admission showed a blood pressure of 120/76 mm of mercury, an irregular pulse of 80 beats per minute and a rectal temperature of 37.9°C (100.2°F). The patient responded only to deep pain. The pupils were equally round and reactive to light. The fundi showed no evidence of papilledema. The neck was rigid with pronounced meningismus, and there was no jugular venous distention to 10 cm at 30 degrees. On examination of the chest diffuse coarse rales and

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rhonchi were noted. First and second heart sounds were normal, but there were a soft apical third heart sound, a grade III/VI systolic ejection murmur at the lower left sternal border and a grade II/VI diastolic decrescendo murmur in the same distribution. The abdomen was distended with no bowel sounds heard; there were no masses. There was prostatic enlargement and a stool specimen was guaiac-positive. Extremities showed 1+ pitting edema. Results of neurological examination were significant for the presence of frontal lobe release signs and oculocephalic reflexes were normal. Corneal and gag reflexes were present. The four extremities moved symmetrically in response to pain, and there was diffuse increase in tone. The deep tendon reflexes were within normal limits. An electrocardiogram showed right bundle branch block with multiple premature atrial contractions. Pulmonary edema was noted on an x-ray film of the chest. A kidney, ureter and bladder study showed a paucity of bowel gas with a nasogastric tube in place, and a prolonged nephrogram phase. An x-ray of the left arm showed an extensive lytic process with an oblique fracture involving the humerus. Laboratory studies gave the following values: hematocrit, 31.6 percent; leukocyte count, normal; sedimentation rate, 140 mm per hour; peripheral blood smear showed rouleaux formation; sodium, 120 mEq per liter; potassium, 5 mEq per liter; bicarbonate, 16 mEq per liter; pH, 7.22; anion gap, 10; calcium, 8.3 mg per dl; phosphate, 7.5 mg per dl; uric acid slightly elevated at 8.6 mg per dl; serum viscosity, 2.2. Analysis of urine showed 2+ proteinuria by dipstick and 4+ proteinuria by 20 percent sulfa salicylic acid. The urine sodium value was 18 mEq per liter. A lumbar puncture and computerized tomography brain scan were entirely within normal limits.

The patient was admitted to the intensive care unit where cultures were obtained and broad-spectrum antibiotics were given. Urine output remained at 10 to 20 ml per hour despite the use of high dose furosemide, and the following day a Scribner shunt was placed in the right forearm. The first of many episodes of hemodialysis was carried out. BUN and creatinine values decreased accordingly. There followed a deterioration in ventilatory status with carbon dioxide retention requiring intubation and mechanical ventilation for 48 hours. The initial diagnosis of multiple myeloma was corroborated by a number of studies, including serum protein electrophoresis which showed 2.6 grams per dl of gamma globulin with a monoclonal spike. Immunoelectrophoresis showed an IgG kappa paraprotein with greater than 2,700 mg per dl IgG and a concomitant suppression of IgM and IgA. Urine protein electrophoresis showed 78 percent gamma globulin fraction, and urine light chains were greater than 1,200 μg per ml. Bone marrow aspirate showed 40 percent to 50 percent plasma cells, some of which were multinucleate. Long bone films showed myeloma involving the right, as well as left humerus, left scapula and clavicle, and findings on skull films were within normal limits.

The patient's pulmonary edema subsequently resolved rapidly with dialysis, mental status cleared gradually over a period of about one week, and he became entirely oriented and alert. Fever abated within 24 hours and administration of antibiotics was discontinued four days after admission when cultures were negative. With continued dialysis over two weeks, the BUN value fell to 35 mg per dl and the creatinine level fell to 2.5 mg per dl; they remained stable at these levels for at least ten days before discharge without dialysis. Spontaneous urine output simultaneously increased to one liter per day. One week after discharge the creatinine value had fallen to 2.1 mg per dl. The patient's multiple myeloma was treated with a four-day course of melphalan and prednisone, which was followed within ten days by a moderate pancytopenia. Outpatient follow-up examinations have since been done by the Medical, Orthopedic and Hematology-Oncology Services and subsequent courses of chemotherapy will be given.

DR. JAMES NAUGHTON:* Renal disease is the second most common cause of death in patients with multiple myeloma.[1,2] As illustrated by today's case, the course at times can be catastrophic and requires the most aggressive supportive care to insure patient survival. Other manifestations of myeloma may be subtle in their effects on the serum electrolytes and on urine protein excretion, and yet may provide very important diagnostic clues. Today, I wish to discuss four syndromes related to abnormalities of renal function in patients with multiple myeloma: (1) serum electrolyte abnormalities, (2) tubular abnormalities, (3) acute renal failure and (4) chronic renal failure.

The first of these syndromes deals with abnormalities of serum chemistry. There have been

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many references to the effect of myeloma proteins on the anion gap.[3,4] I prefer to calculate the anion gap simply by adding the serum chloride and bicarbonate values, and subtracting the sum from the serum sodium level. In order to simplify the arithmetic I do not use the serum potassium value in the calculations. The normal value for the anion gap is on the order of 12 mEq per liter with a standard error of about 0.5 mEq per liter.[3] These unmeasured anions are accounted for by the serum proteins, chiefly albumin, which are negatively charged; that is, they are anionic at physiologic pH. Albumin makes up about 75 percent of the normal anion gap. Immunoglobulins, particularly IgG, differ from albumin in that they are positively charged at the physiologic pH of serum. Therefore, if immunoglobulins accumulate in the blood, there will be a reduction in the calculated anion gap. Concomitant decrease in the serum albumin would further accentuate this decrease. In a review of this subject by Murray, the average anion gap in 50 patients with multiple myeloma was 9.2 mEq per liter, compared with 12.2 mEq per liter in controls.[3] This is statistically significant, although not so helpful clinically. However, almost a third of the patients with myeloma in that report had anion gaps less than 6 mEq per liter. This is several standard deviations away from the normal. Only two or three clinical entities can cause this: multiple myeloma, bromide poisoning—which has a completely different clinical presentation than myeloma—and some cases of severe hypernatremia which, of course, are already eliminated by initial measurement of the serum electrolytes.

The case presented today provides an interesting twist on the above observation. On admission the patient had a serum sodium level of 120 mEq per liter, a bicarbonate value of 16 mEq per liter and a serum chloride value of 94 mEq per liter. These yield an anion gap of 10 mEq per liter, very close to the normal range. However, the patient was in acute renal failure; the creatinine level was 7.8 mg per dl and metabolic acidosis was present with a pH of 7.22. This clinical situation should have resulted in an elevated anion gap, so the first diagnostic clue as to the underlying disorder could be obtained from the electrolyte determinations done on admission. When the acute renal failure with metabolic acidosis resolves there should be a reduced anion gap. This is exactly what happened. At the time of discharge the patient's anion gap was 5 to 6 mEq per liter. Before leaving the anion gap I want to point out that the same physiochemical properties of immunoglobulins that give rise to the narrowing of the anion gap also account for their failure to react with the urine indicator dye reactions for protein (dipstick). That reaction requires the presence of an anionic protein such as albumin. This will buffer hydrogen ions and cause a specific chemical reaction to produce the colorimetric change that identifies the presence of protein in the urine. Cationic proteins, including light chains, do not buffer hydrogen ion and therefore do not react.

The patient presented today provides a splendid example of the diagnostic information obtained by comparing the urine dipstick reaction and the sulfa salicylic acid reaction. The urine dipstick reaction was only weakly positive, whereas the sulfa salicylic acid reaction, which nonspecifically precipitates any protein, was grossly positive, suggesting the presence of cationic protein (immunoglobulin) in the urine. These two pieces of information, the inappropriately narrow anion gap and differential reaction for urine protein, strongly suggest the diagnosis of multiple myeloma.

Occasionally in patients with myeloma there will be a reduced serum sodium concentration; this factitious hyponatremia may even contribute to the reduction in the anion gap. There are two mechanisms by which this may occur. The first is simply the displacement of salt and water from any given aliquot of the serum by a large amount of paraprotein in the serum. This is entirely analogous to the hyponatremia seen with certain hyperlipoproteinemias. The other, and less common, difficulty with the measurement of the serum sodium occurs when there is co-existent hyperviscosity. This most frequently occurs in Waldenstrom macroglobulinemia, or with IgA myeloma wherein immunoglobulin molecules may polymerize. It rarely occurs in IgG myeloma. This is purely a technical problem related to the instrument used in the laboratory to measure the serum sodium level which uses an automated aspirating pump.[4] When the viscosity of the serum is elevated, the pump fails to aspirate the appropriate amount of serum, so it measures a smaller amount of sodium. Since the chloride is not measured by that same automated pump, its measured value may be normal. This will also result in an apparent lowering of the anion gap as well as hyponatremia, and can be corrected by having the laboratory manually pipette the serum sodium sample

TABLE 1.—*Renal Tubular Abnormalities in Myeloma*

Bence-Jones proteinuria
Light chains, molecular weight 20,000 daltons, filtered at glomerulus, normally reabsorbed *and* catabolized by renal tubules.
Appearance in urine may signify *either* overproduction and saturation of reabsorptive mechanism (myeloma) *or* renal tubular disease ("tubular proteinuria" systemic lupus erythematosus).
Light chains dimerize in acid pH to form Bence-Jones protein (molecular weight 40,000 daltons).
Proximal tubule dysfunction—Fanconi syndrome (glycosuria, phosphaturia, uricosuria, aminoaciduria).
Rare—about 15 cases, antedates clinical onset of myeloma.
Distal tubule dysfunction
Nephrogenic diabetes insipidus—in absence of hypercalcemia; only occurs in presence of Bence-Jones proteinuria.
Distal (gradient limited) renal tubular acidosis—only apparent with acid loading; correlates with presence of Bence-Jones protein.

in the presence of hyperviscosity. In the case discussed today, blood viscosity was determined; it was only minimally elevated and therefore was not contributing to the patient's low anion gap. The hyponatremia was not factitious and was a consequence of the patient's acute renal failure.

Hypercalcemia due to increased bone breakdown occurs during the course of myeloma in 50 percent to 60 percent of patients.[1] It may have profound consequences on renal function as well as on central nervous system function. Hyperuricemia also occurs, particularly after the initiation of treatment. This must be kept in mind and managed prophylactically to avoid the renal sequelae.

I shall turn now to consider some of the tubular abnormalities that may occur in myeloma (Table 1). In 1847 Henry Bence-Jones published a paper entitled "A new substance appearing in the urine of a patient with mollities ossium."[5] It may interest you to know that mollities ossium is not an antiquated term for multiple myeloma; it is an antiquated term for osteomalacia. Bence-Jones was not the first to observe this "new substance in the urine" but simply confirmed the observations of two others and published it first.[6] We know now that the proteinaceous precipitate that he observed when he warmed the urine of his patient to about 55°C, only to see it disappear with further heating, represents a dimer of light chains, either kappa or lambda, often found in patients with paraprotein disorders. Light chains are normally produced some 40 percent in excess of heavy chains. Light chains have a molecular weight on the order of 20,000 daltons and as such they are relatively well filtered at the glomerulus. Waldmann and his colleagues have shown that filtered light chains are reabsorbed and catabolized by the renal tubules.[7] Their appearance in the urine reflects either overproduction to the extent that the reabsorptive capacity is overwhelmed or a defect in tubular function.

We commonly make use of this information in two ways: the overproduction states such as multiple myeloma are associated with light chain (Bence-Jones) proteinuria; impaired tubular reabsorption may occur in patients with renal diseases such as lupus nephritis. Serial determinations of urinary light chain excretion may be useful in following the course of patients with lupus nephritis.[8] In the presence of an acid pH, light chains will form dimers which are less soluble. These dimers with molecular weights on the order of 40,000 daltons are what we recognize as the Bence-Jones protein. The less soluble dimerized form may precipitate in the tubules and cause tubular obstruction. This is the primary pathogenesis of chronic renal failure in myeloma, that is, myeloma kidney. It is uncertain whether excessive concentrations of light chains are directly toxic to tubular function independent of their mechanical obstructive properties. Preuss and his associates have shown that proteins extracted from the urine of patients with multiple myeloma are directly inhibitory to tubular transport functions in isolated rat kidney slices, whereas proteins extracted from the urine of patients with nephrotic syndrome are not inhibitory.[9] This would support the idea that light chains may be directly toxic to tubular function.[10] On the other hand, any disease process damaging renal tubules could be associated with an increase in light chain excretion. At present, this question is unresolved.

Several clinical conditions have been identified in which increased light chain excretion has been associated with tubular dysfunction.

Proximal tubular dysfunction has now been documented in some 15 patients with multiple myeloma presenting as a full-blown, adult-acquired form of the Fanconi syndrome.[11] In several of these cases, renal biopsy studies have shown the presence of large crystalline, electron dense deposits in proximal tubular cells, corresponding to similar crystalline dense deposits in the plasma cells of these patients. This is a rare finding and in only a handful of the 15 reported cases

TABLE 2.—*Acute Renal Failure in Multiple Myeloma*

Frequency: Approximately 7.5 percent (may be presenting manifestation of myeloma)
Causes:
Urography—rare (1 percent)
Hypercalcemia
Dehydration
Antibiotics
Sepsis
Prognosis: recovery frequent

have the appropriate histologic studies been done. It has been suggested that these deposits represent crystals of light chains, which accumulate in proximal tubule cells as a consequence of increased plasma cell production and reabsorption following glomerular filtration. They may be responsible for the multiple tubular transport defects seen in these patients.[11] Interestingly, these patients with the Fanconi syndrome did not have clinically obvious myeloma when they first presented. They had a pronounced increase in light chain excretion, symptoms of the Fanconi syndrome—generally weakness associated with hypophosphatemia—and all of the other associated tubular transport defects. Over a period of years, overt myeloma developed. This could be due to structurally different paraproteins that cause tubular toxicity when the overall tumor mass is much lower than in the usual case of overt myeloma.

Distal tubular dysfunction has also been reported in patients with myeloma and Bence-Jones proteinuria.[12] Nephrogenic diabetes insipidus in the absence of hypercalcemia may occur in the presence of Bence-Jones proteinuria and distal renal tubular acidosis has also been shown to be present in patients with myeloma.[12] Both of these defects have generally not been clinically obvious; that is, the patients were not polyuric, the concentrating defect was only shown when water intake was restricted and they were not clinically acidotic. Their urine acidification defect was only manifest when they were challenged with an acid load. Whether these last two defects which are clinically silent are the result of increased light chain excretion or simply an association remains to be determined.

We now move to the syndrome of acute renal failure (Table 2). The frequency of acute renal failure during the course of myeloma is unknown. The only large series in the literature is by DeFronzo and his associates. They reported 14 cases of acute renal failure which developed during the course of 187 cases of myeloma, a frequency of 7.5 percent.[13] As in the case discussed today, several patients have presented at the University of California, San Francisco, with acute renal failure as the initial manifestation of myeloma. Intravenous pyelography as a precipitating cause of acute renal failure in myeloma has been widely discussed since the original report by Bartel in 1954.[14] Several large retrospective reviews of patients with myeloma in whom pyelography has been carried out, indicate that the incidence of acute renal failure is approximately 1 percent.[15,16] Among the mechanisms suggested as the cause of acute renal failure are dehydration as a result of the bowel cathartics given before the radiographic procedure, osmotic diuresis from the contrast agent leading to dehydration and cast precipitation, urate deposition in tubules secondary to the uricosuric effect of radiographic dyes[17] and direct dye-induced protein precipitation. The radiographic dyes in use do not precipitate Bence-Jones proteins *in vitro*. However, angiographic dye may cause the precipitation of the so-called Tamm-Horsfall proteins, the tubular secretory proteins.[18] These proteins may begin to precipitate and cause tubular stasis and lead to precipitation of Bence-Jones protein with resultant tubular occlusion. Finally, direct vascular effects of the dye may cause vasospasm in the kidney, a low flow state, hyperconcentration of the protein within the filtrate and precipitation.[19]

On renal biopsy, these patients often are found to have extensive cast deposition within the renal tubules, unlike the acute tubular necrosis reported with angiographic procedures in other clinical situations. This suggests that the dye must play a role in the precipitation of Bence-Jones protein.

Other factors must be kept in mind, however, and may be more important than the role of pyelography in the development of acute renal failure in myeloma. In the review by DeFronzo only one of 14 cases of acute renal failure was associated with pyelography, whereas factors such as hypercalcemia, antibiotic toxicity and sepsis were more common.[13] Hypercalcemia has two effects: it can be directly nephrotoxic—through the mechanism of producing nephrocalcinosis—or it may induce the state of nephrogenic diabetes insipidus, a concentrating defect which predisposes the patient to dehydration and protein precipitation in the tubules. If acute renal failure develops in this setting, what is the prognosis? Most of the reports in the literature are not encouraging. In DeFron-

TABLE 3.—*Causes of Chronic Renal Failure in Myeloma*

"Myeloma kidney": tubular obstruction secondary to precipitations of Bence-Jones proteins, by far the most common lesion
Hypercalcemia—40 percent to 60 percent
Hyperuricemia
Amyloidosis—10 percent
Plasma cell invasion of kidneys—rare
Pyelonephritis

zo's series, nine of 14 patients died during the period of acute renal failure, and four of the remaining five died within two months.[13] However, that was a retrospective study garnered over a decade (from 1963 to 1973) which included a period where the aggressive dialytic support of patients with an underlying malignancy was less common.

At the University of California, San Francisco, we have seen three patients in the last two months with acute renal failure and multiple myeloma. In each instance, acute renal failure was the presenting manifestation of the disease. The only patient in whom an intravenous pyelogram was done was in the case presented today. Each of those three patients has recovered renal function after a period of hemodialysis and is now off dialysis and functioning out of hospital. Recent experience at the Mayo Clinic also supports a favorable outcome.[1]

Table 3 provides a differential diagnosis of the appearance of azotemia in a patient with myeloma. The most common cause is the first one—so-called "myeloma kidney," with a characteristic biopsy finding of tubulointerstitial disease with large, eosinophilic "hard" casts. These casts may appear laminated or fractured. They often provoke a proliferative response in the tubular epithelial cells with giant cell and syncytial formation. These casts are reportedly the longest seen in any renal disease and may occupy the full length of the nephron from proximal tubule to collecting duct. They predominantly contain Bence-Jones protein with some intact immunoglobulin, fibrinogen and Tamm-Horsfall protein.[20] The pathogenesis of myeloma kidney involves the filtration of light chains, dimerization of the light chains in the acidic urine leading to frank precipitation and trapping of various proteinacious elements within the tubules. There may be additional interstitial reaction and scarring and some secondary glomerular ischemia. Dehydration would accelerate this process by causing higher concentrations of protein in the filtrate. There are two experimental models to support this. In one model Bence-Jones proteins are parenterally injected into mice.[21] The other model involves innoculating mice with plasma cell tumors that secrete light chains. In this latter model, Bryan and McIntire have shown good correlation between tumor mass, the number of tubules containing casts and renal function.[22] Dehydrating these animals causes increased cast formation; maintaining a sustained diuresis with furosemide decreases cast formation. These results lend credence to our clinical impression that the state of hydration is indeed an important variable in the development of myeloma kidney.[22]

Hypercalcemia leads the other treatable causes of renal failure in myeloma (Table 3). An elevated serum calcium level occurs in 40 percent to 60 percent of myeloma cases at some point in the illness. Some degree of nephrocalcinosis is frequently present in biopsy specimens. Treatment of hypercalcemia in myeloma should first begin with a saline diuresis if tolerated, followed by prednisone. This is one of the hypercalcemic disorders that is quite responsive to prednisone therapy. Mithramycin is also effective in the more severe cases. Hyperuricemia, occurring primarily after the introduction of chemotherapy, can be prevented by prophylactic treatment with allopurinol and maintaining hydration. The dose of allopurinol should be reduced in those patients with significant renal insufficiency. Amyloidosis can be detected in about 10 percent of renal autopsy specimens in patients dying with multiple myeloma.[20] The protein deposited in primary amyloidosis consists of light chains. Primary amyloidosis is now considered part of the spectrum of plasma cell dyscrasias,[23] In myeloma, amyloid accumulation rarely impairs renal function. Clinically, the development of the nephrotic syndrome in a patient with myeloma suggests significant amyloidosis.[2] It carries no particular therapeutic implication as the treatment of the underlying disorder remains the same. Direct plasma cell invasion of the kidney has also been described. This appears even less common than amyloidosis and is almost never detected antemortem.[20] In a few cases massive retroperitoneal infiltration with plasma cells occurred and obstructive uropathy resulted.

Infection is the leading cause of death in cases of myeloma.[1] The urinary tract is a frequent site of infection and great care should be taken to avoid instrumentation in these high risk patients.

TABLE 4.—*Treatment of Renal Failure in Multiple Myeloma*

General principles: avoid dehydration, urinary tract instrumentation.
Treat hypercalcemia, hyperuricemia (expectantly)
Cautious use of nephrotoxic antibiotics
Intravenous pyelography if indicated
Specific treatment: forced diuresis and alkali therapy have been suggested, no controlled data.
Dialysis: both acute and chronic.
Four of seven patients in recent series survived longer than one year
Renal transplantation: may be considered in stable patients who have achieved remission with chemotherapy

While a urinary tract infection should always be considered a likely source of sepsis in these patients, it is a rare cause of renal failure.

I would like to briefly comment on renal insufficiency in Waldenstrom macroglobulinemia. It differs from multiple myeloma in that the predominant renal lesion is glomerular, not tubular. It consists of the accumulation of large hyaline thrombi on the capillary lumen.[24] Immunofluorescence staining shows these deposits to be primarily composed of IgM. Tubular casts are uncommon and not nearly so widespread in Waldenstrom macroglobulinemia as they are in myeloma. Treatment is directed at the primary disorder.

In all of these disorders, then, histologic examination of the kidney is not likely to change the treatment. Except in most atypical situations, a renal biopsy study need not be done in patients with multiple myeloma.

In considering treatment (Table 4), a few general principles are important: avoid dehydration which may lead to excessive cast formation and avoid urinary tract instrumentation in these infection-prone patients. Hypercalcemia and hyperuricemia are among the most treatable sequelae of myeloma and they should be aggressively pursued. Nephrotoxic antibiotics have been implicated in a significant number of patients in whom renal failure develops with myoloma. It has been suggested that in the presence of Bence-Jones proteinuria, antibiotic toxicity may be enhanced.[13] There is no direct evidence to support this, but nephrotoxic antibiotics should be administered at reduced doses in those patients who have renal insufficiency. Serum levels should be monitored. Pyelography does not pose an undue risk to patients with myeloma in whom hydration is adequate. However, if the diagnosis of myeloma is made, there is really no indication for an intravenous pyelogram in a vast majority of cases. The presence of the paraprotein disorder is a sufficient explanation for renal insufficiency. If obstructive symptoms also are present, or there are physical findings suggestive of urinary tract obstruction, then a pyelogram carried out with adequate hydration is a reasonable diagnostic procedure. Under these conditions, the incidence of acute renal failure may be kept to 1 percent.

There is evidence from both animal studies and several anecdotal clinical reports that forced diuresis and alkalization of the urine will prevent or ameliorate myeloma kidney.[21,22,25] There are no controlled clinical data. In patients who can tolerate sodium loading, the ingestion of 3 to 4 liters of fluid per day and about 10 grams of sodium bicarbonate has been recommended as possibly beneficial in the face of developing renal insufficiency and documented Bence-Jones proteinuria.[25]

There is growing experience with both acute and chronic hemodialysis in patients with multiple myeloma. We would consider patients in whom acute renal failure develops to be suitable for dialysis if they are otherwise candidates for continuing treatment of their myeloma. Our recent experience suggests that they have a reasonable chance to recover renal function and not require long-term dialysis. There are also several reports of patients with myeloma doing well on programs of long-term dialysis. In a recent series by Vaziri and his colleagues, four of seven patients receiving long-term dialysis survived for at least a year, and two of seven were alive after three years.[26] It appears that patients with myeloma whose only major disability is renal failure and in whom additional chemotherapy is planned can be considered for long-term hemodialysis. Their tolerance for chemotherapy appears to be significantly improved when a program of long-term dialysis is being carried out.

There have been a very few case reports of renal transplantation in patients with myeloma and chronic renal failure.[27] In these patients hemodialysis had been maintained and remission of myeloma was achieved with chemotherapy. This is a most unusual combination of events. One such patient has received a renal transplant at this medical center. The diagnosis of multiple myeloma was established two years before transplantation, renal failure developed as a result of the myeloma, the patient was maintained on he-

modialysis and there was a complete hematologic remission on chemotherapy. A kidney was transplanted from a cadaver and the patient is doing well a year and a half after the transplant without recurrence of the myeloma. The age of patients with myeloma places many of them beyond the 60-year age limit for transplant candidates accepted by our Kidney Transplant Service.

In the case discussed today there were abnormalities in each of the four areas I have outlined. The patient had a reduced anion gap, he was hypercalcemic and hyperuricemic. He had Bence-Jones proteinuria, and acute renal failure developed superimposed on chronic renal failure. The excellent care provided by the house staff shows that in spite of his advanced age and underlying malignant condition it is possible to restore a satisfactory quality of life to someone this severely afflicted.

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